b) identifying an agent which binds to the fungal TIM17,

c) combining the agent with the human mitochondrial membrane protein of claim 17, and

d) determining that the agent does not bind to the human mitochondrial membrane protein, thereby identifying the agent with antifungal specificity.

43. (Reiterated.) A method for identifying a specific antiprotozoal agent, the method comprising:

a) combining at least one agent with a protozoal TIM17,

b) identifying an agent which binds to the protozoal TIM17,

c) combining said agent with the human mitochondrial membrane protein of claim 17, and

d) determining that said agent does not bind to the human mitochondrial membrane protein, thereby identifying the agent with antiprotozoal specificity.

REMARKS

Claims 2-10 and 17-43 are pending in the application. Claims 2-10 have been canceled. Claims 19-31 and 34-43 are withdrawn as being drawn to non-elected inventions. Applicants reserve the right to prosecute the non-elected claims in subsequent divisional applications. Claims 17 and 32 have been amended to further clarify the intended subject matter of the claimed invention. No new matter has been added by these amendments. Entry of these amendments is respectfully requested.

Withdrawal of previous rejections:

Applicants thank the Examiner for withdrawing the rejection of claims 17 and 18 under 35 U.S.C. 112, second paragraph. Applicants believe that with the amendments offered in this response and the remarks made herein, the remaining rejections should also be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph for alleged lack of enablement:

The rejection of claims 32 and 33 under 35 U.S.C. § 112, first paragraph for alleged lack of enablement was maintained. The Examiner asserts that "there is still uncertainty as to what function is to be achieved by an 'effective amount'." (Office Action, page 3.) Applicants respectfully point out that the specification discloses that the claimed polypeptides may be used in the diagnosis, prevention, and treatment of conditions including cancer and disorders associated with parasitic and fungal infections, specific examples of which are listed on pages 24-25 of the specification.

However, in the interest of expediting the prosecution of the instant application, Applicants have amended claim 32 to delete the recitation of the phrase "an effective amount". Therefore, the Examiner is respectfully requested to withdraw the rejections of claim 32 and dependent claim 33 under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, first paragraph for alleged lack of written description:

The rejection of claims 17 and 18 under 35 U.S.C. § 112, first paragraph, for alleged lack of adequate written description was maintained. The Examiner asserts that despite the amendments to claim 17, "there is still no disclosure of the genus of polypeptides that the claim reads on and those subgenera still would have varying characteristics" (Office Action, page 4). Applicants respectfully traverse.

As discussed in the previous response, claim 17 has been amended to recite specific functional attributes required of the claimed fragments, and these activities can be determined using assays disclosed in the specification. The Examiner concedes that these assays "would provided information on whether or not the subgenera displayed a specific activity or function" (Office Action, page 4). These activities are the characteristics used to define the classes of claimed fragments; thus these subgenera are well defined. It is unclear why some larger genus of polypeptides needs to be disclosed when the claims encompass only the more limited and well described subgenera. While there may be an "infinite" number of polypeptide fragments that could be derived from SEQ ID NO:1, the claims are directed to this more limited, well defined

set. Thus one of skill in the art would reasonably understand the subject matter encompassed by the claims and that Applicants were in possession of the claimed invention at the time of filing. Withdrawal of the rejections of claim 17 and dependent claim 18 under 35 U.S.C.§ 112, first paragraph, is therefore respectfully requested.

Rejections under 35 U.S.C. § 112, second paragraph:

The rejection of claims 32 and 33 under 35 U.S.C. § 112, second paragraph for allegedly being indefinite was maintained. The Examiner asserts that the phrase "effective amount" in claim 32 is vague and indefinite when the claims fail to state the function which is to be achieved. As discussed above, Applicants respectfully point out that the purpose of the effective amount is clear when read in light of the specification, which discloses that the claimed polypeptides are useful for the diagnosis and treatment of conditions including cancer and disorders associated with parasitic and fungal infections. However, in the interest of expediting the prosecution of the instant application, Applicants have amended claim 32 to delete the recitation of the phrase "an effective amount". Therefore, the Examiner is respectfully requested to withdraw the rejections of claim 32 and dependent claim 33 under 35 U.S.C. § 112, second paragraph.

Claims 17 and 18 are newly rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. The Examiner asserts that the recitation of "HuMIM17" or "HuTIM17" in the claims is vague and indefinite because these abbreviations are not well known in the art. Applicants thank the Examiner for noticing that "HuMIM17" recited in claim 17 should have correctly been "HuTIM17". The abbreviation TIM17 is an art-recognized term which refers to the translocase of inner mitochondrial membrane 17, as disclosed in the specification (at, for example, page 1, lines 14-16; and page 1, line 25 through page 2, line 6). However, in the interest of expediting the prosecution of the instant application, Applicants have amended claim 17 to include the full terminology as suggested by the Examiner. Withdrawal of the rejection of claim 17 and dependent claim 18 under 35 U.S.C. § 112, second paragraph is therefore respectfully requested.

Rejections under 35 U.S.C. §§ 101/112, first paragraph:

The rejection of claims 17 and 18 under 35 U.S.C. §§ 101 and 112, first paragraph for alleged lack of utility was maintained. The Examiner asserts that the uses asserted by Applicants in toxicology testing, drug development, and disease diagnosis are unconvincing since there is "no objective evidence of record to show that HuTIM17 can be used in the treatment of infections by protozoan parasites, as well as disorders caused by AIDS and cancer," and additionally that "mere expression in a tissue does not mean treatment." (Office Action, pages 5-6.)

Applicants respectfully point out that the asserted utilities for HuTIM17 are not limited to treatment of cancers or parasitic and fungal infections, but include, for example, expression profiling, toxicology testing, and drug discovery. For example, the specification discloses that the claimed HuTIM17 polypeptides may be used to identify new antifungal or antiprotozoal agents by screening for agents that bind to the parasite or fungal TIM17 but not the human protein (page 24, line 27 through page 25, line 18). TIM proteins are known to play essential roles in the import of proteins from the cytoplasm into mitochondria, with depletion of TIM17 causing defects in the import of several mitochondrial proteins (specification, pages 1-2). TIM17 is one of the few proteins essential for yeast viability (specification, page 2, lines 4-6), demonstrating the importance of its function and confirming its utility as a drug target in other fungal organisms.

The Examiner also asserts that the use for the claimed products as tools for toxicology testing and drug discovery is insufficient since "'[t]ools' are merely used to 'hunt' with and do not provide any successful conclusion." (Office Action, page 6). As discussed in the previous response, there is no authority for the proposition that use as a tool for research is not a substantial utility. Only a limited subset of research uses are not "substantial" utilities: those in which the only known use for the claimed invention is to be an **object** of further study, thus merely inviting further research. Despite the assertions of the Examiner, *Brenner v. Manson* did not even address the issue of whether use as a **tool** for research was a substantial utility. The text of the case makes clear that the relevant issue was that "Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of

use-testing" (*Brenner*, p.696). Nowhere does this case state or imply, however, that a material cannot be patentable if it has some other beneficial use in research, nor does the Examiner provide any evidence for this view aside from a bald statement of opinion.

Applicants also respectfully point out that, contrary to the Examiner's assertions, the claimed HuTIM17 polypeptides are useful in toxicology testing and expression profiling even if the so-called "therapeutic" function of HuTIM17 is not known. In the case of toxicology testing, for example, it is important to determine that a drug designed to affect a specific target does not produce additional effects on other molecules, particularly those known to be associated with basic cellular processes, such as protein transport. Since TIM17 proteins have essential roles in mitochondrial import, the HuTIM17 polypeptides would be a useful control to screen drugs so as to determine which ones did not affect this important cellular process. No further experimentation would be required to utilize the the TIM17 polypeptides in this way.

The Examiner also argues that "characterizations based on structural/functional relationships have many problems" (Office Action, page 7), citing the paper by Bork in support of this statement. Applicants respectfully suggest that the Examiner attempts to draw too sweeping conclusions from Bork. It may be true that the use of sequence analysis to predict protein function is not 100% percent accurate (although still, based upon Bork's figure of 70% accuracy, more likely than not to be correct) as the quality of data in the public sequence databases is still insufficient to perfectly annotate every new sequence. However, this is a general conclusion; one of skill in the art would clearly understand that the likelihood of a prediction being correct for a particular sequence depends upon how much data is available for the particular family to which it belongs. HuTIM17 has strong amino acid homology to both yeast TIM17 and human preprotein translocase. In addition, HuTIM17 and yeast TIM17 have similar hydrophobicity plots, and HuTIM17 has three potential transmembrane domains (specification, page 12, lines 10-20). Thus based on all the evidence of record, one of ordinary skill in the art would reasonably believe that HuTIM17 is indeed a member of the TIM17 family of mitochondrial import proteins.

Based upon all the above evidence and arguments, as well as those presented in the previous Response, Applicants have clearly provided sufficient evidence for the stated utilities of

the claimed polypeptides in expression profiling, toxicology testing, and the development of drugs for the treatment of fungal and parasitic infections. Withdrawal of the rejections of claims 17 and 18 under 35 U.S.C. §§ 101/112, first paragraph is therefore respectfully requested.

Rejections under 35 U.S.C. §§ 102/103:

The rejection of claim 17 under 35 U.S.C. 102(b) as allegedly anticipated by various references including Accession Numbers P39515, Q02310, Maarse et al., Ryan et al., and U.S. Patent #5,876,991 was maintained. The rejection of claim 32 under 35 U.S.C. 103(a) as allegedly being unpatentable over the above references in view of Harlow and Lane was also maintained. The Examiner asserts that although claim 17 was amended to recite a biologically active fragment of SEQ ID NO:1 having HuTIM17 activity, this recitation does not distinctly claim the fragments because the abbreviation HuTIM17 does not describe the activity of the claimed polypeptides.

Applicants respectfully point out that the abbreviation HuTIM17 has been defined in the specification, and that the activity assays disclosed in the specification are clearly designated as demonstrations of HuTIM17 activity. However, in order to clarify the intended subject matter of the claimed invention, Applicants have amended claim 17 to recite fragments having translocase of inner mitochondrial membrane 17 activity. This claim language incorporates the full terminology for which TIM17 is an abbreviation, as disclosed in the specification at, for example, page 1, lines 14-16; and page 1, line 25 through page 2, line 6. The function of TIM17 is known to be in import of proteins from the cytoplasm into the mitochondria. The activity of the claimed fragments may be assayed using the assays disclosed in Example IX, pages 46-47, which measure the import of HuTIM17 into the inner mitochondrial membrane. Applicants respectfully point out that the reference fragments, derived from yeast MIM17, would be no longer than six amino acid residues (see the alignment between yeast MIM17 (GI557267) and HuTIM17 as shown in Figure 2), and thus would lack the transmembrane domains required for successful insertion into the mitochondrial membrane. Thus the cited references do not disclose the claimed fragments having the recited activity, and therefore fail to anticipate claim 17. Nor are compositions comprising the fragments, as in claim 32, made obvious by the references in

view of Harlow and Lane, since Harlow and Lane is a general reference on antibody methods and does not disclose the claimed fragments. The withdrawal of the rejections of claims 17 and 32 is therefore respectfully requested.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact Applicants' Attorney at (650)855-0555.

Applicants believe that no fee is due with this communication. However, if the USPTO determines that a fee is due, the Commissioner is hereby authorized to charge Deposit Account No. **09-0108. This form is enclosed in duplicate.**

Respectfully submitted,

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